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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,191	11/20/2001	D. Wade Walke	LEX-0270-USA	4055

7590 07/25/2003

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EXAMINER	
DEBERRY, REGINA M	
ART UNIT	PAPER NUMBER
1647	9

DATE MAILED: 07/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,191	WALKE ET AL.	
	Examin r	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 May 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Status of Application, Amendments and/or Claims

The amendment filed 19 May 2003 (Paper No. 7) has been entered in full. New claim 5 and 6 were added. Claims 1-6 are pending.

The information disclosure statement filed 19 May 2003 (Paper No. 8) was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Withdrawn Objections And/Or Rejections

The rejection of claims 2 and 4 under 35 USC 112, second paragraph, as set forth at pages 6-7 of the previous Office Action (20 February 2003, Paper No. 6) is *withdrawn* in view of the amendment (19 May 2003, Paper No. 7).

Claim Rejections - 35 USC § 101

Claims 1-6 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility. The basis for this rejection is set forth at pages 2-6 of the previous Office Action (20 February 2003, Paper No. 6).

Applicant states that the references used to support the position that different Wnt-family member proteins have different functions is irrelevant to the utility of the

sequence claimed in the present application. The specification as originally filed characterizes the claimed sequence, not just as a random member of the Wnt-family of molecules, but specifically Wnt-14 (page 20, lines 16-17). Applicant states that a sequence sharing over 99% identity at the protein level with the claimed sequence has been annotated as homo sapien mRNA for WNT 14. Applicant submits Exhibit C. Applicant maintains that the specification as originally filed states that the presently claimed sequence has a role in cancer as well as a role in development. Applicant submits Exhibits D and E.

Applicant's arguments have been fully considered but not deemed persuasive. Kirikoshi *et al.* (Exhibit D) teach the expression of WNT 14 in human cancer. Kirikoshi specifically teaches that WNT 14 mRNA was detected in 7 out of 7 pancreatic cancer lines, 12 out of 12 esophageal cancer lines, 4 out of 4 cervical cancer lines, and 5 out of 7 brain tumor cell lines. Hartmann *et al.* (Exhibit E) specifically teach that WNT 14 plays a central role in initiating synovial joint formation in the chick limb. Hartmann *et al.* teach that WNT 14 is expressed in joint forming regions prior to the segmentation of the cartilage elements. The instant specification does not disclose a specific cancer cell lines where WNT 14 is exclusively expressed, nor does it disclose a developing skeleton function. The specification states that WNT 14 has a role in cancer, however they are many forms of cancer. It is well known in the art that cancers such as breast, colon and ovarian have very different etiologies. The specification does not specifically teach the role WNT 14 plays in cancer. Does the overexpression of WNT 14 cause cancer (i.e. oncogene) or the underexpression (i.e. tumor suppressor gene).

Furthermore, tumor cell lines are not equal to tumor tissue. The cell culturing process alters gene expression and selects subgroups of cells, such that the cultured cells are not longer representative of the diseased tissue. Tumor cell lines are usually analyzed by polymerase chain reaction (PCR). Insignificant expression levels are amplified until they appear significant. The specification states that WNT 14 has a role in development. The specification fails to teach if development means that WNT 14 affects growth and/or differentiation. The specification fails to teach specific areas of development. For the reason listed above, the specific utilities were not asserted in the specification as originally filed in view of Kirikoshi *et al.* and Hartmann *et al.*

Applicant maintains that only one credible assertion of utility has to be made to meet the requirements of 35 USC 101. Applicant cites case law. Applicant contends that polymorphisms are the basis for forensic analysis, which does not require any information about the function of the encoded protein and is undoubtedly a real world utility; the present sequences must in themselves be useful. Applicant states that the present nucleotide sequences have a specific utility in identification of protein coding sequences and mapping a unique gene to a particular chromosome, chromosome 1. SEQ ID NO:1 can be used to map the 4 coding exons on chromosome 1. Applicant submits Exhibit F. Applicant contends that the present polynucleotide provides specificity in localizing the specific region of human chromosome 1 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences.

Applicant's arguments have been fully considered but not deemed persuasive. A polymorphism does not necessarily mean that the change in amino acid will affect activity or cause a disease or condition. Furthermore, the specification fails to teach a correlation between the polymorphism and a disease or disorder. Contrary to Applicant's assertion, mapping a region on human chromosome 1 is not specific to the instant invention because any chromosome region 1 gene can be used to map the particular area of the chromosome.

Applicant informs the Examiner that only a minor percentage of the genome actually encodes exons, which in turn encode amino acids. Applicant states that the specification details that sequences derived from regions adjacent to intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations with the exons, introns, splice sites, that can be used in diagnostics and pharmacogenomics. Applicant states that the Examiner seems to be confusing the requirements for a specific utility, which is the proper standard for utility under 35 USC 101, with that of a unique utility, which is clearly an improper standard. Applicant states that the present nucleotide sequences have utility in assessing gene expression patterns using high-throughput DNA chips. Applicant contends that the present nucleotide sequences are specific markers of the human genome, and such specific markers are targets for the discovery of drugs that are associated with human disease.

Applicant's arguments have been fully considered but not deemed persuasive. Many polynucleotides are known in the art to encode polypeptides, yet the polypeptides

have no known function or known ligands. Furthermore, a specific utility is a utility that is specific to the subject matter claimed which contrasts with a general utility that would be applicable to the broad class of the invention. The specification cites the use of WNT 14 nucleotide sequences in high-throughput chip format. As was stated in the last Office Action, without a disclosure of a particular disease state in which the claimed polynucleotides are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression monitoring assay mean.

Applicant states that the Examiner's argument, "without a disclosure of a particular disease states in which the claimed polynucleotides are expressed at an altered level or form, it would be impossible to determine what the results of a gene expression monitoring assay mean", is misplaced. Applicant maintains that expression profiling does not require a knowledge of disease states in which expression of the selected nucleic acid is increased or decreased, rather the gene chip indicates which DNA fragments are expressed at greater or lesser levels in two or more particular tissue types. Applicant points out that nucleic acid sequences such as SEQ ID NO:1 are routinely used by companies throughout the biotechnology sector exactly as it is presented in the sequence listing, without any further experimentation.

Applicant's arguments have been fully considered but not deemed persuasive. It is unclear what it would mean if a gene chip indicated that a particular DNA fragment is expressed at a greater level in two or more particular tissue types. The asserted utility in gene expression monitoring assays is not substantial, because significant further research would have to be conducted to determine which gene regulating activity,

condition, disease or biological mechanism correlated with altered forms or levels of the claimed polynucleotides. However, an assay that measures the presence of a material, which has a stated correlation to a predisposition to the onset of a particular disease or condition, would be a practical use of the material. Furthermore, nucleic acid sequences such as SEQ ID NO:1 may be routinely used by companies throughout the biotechnology sector, without any further experimentation. The guidelines however are different for obtaining a patent on an invention. A specific and substantial asserted utility or a well established utility amounts to more than a starting point for further research and investigation. It does not require or constitute carrying out further research to identify or reasonably confirm what the practical use might ultimately be.

Applicant states that the association of a particular disease with the claimed sequence is not the standard required for utility under 35 USC 101. Applicant cites In re Brana. Applicant states that even if, arguendo, further research might be required in certain aspects of the present invention, this does not preclude a finding that the invention has utility, as set forth by the Federal Circuit's holding in Brana, which clearly states that pharmaceutical inventions, necessarily includes the expectation of further research and development. Applicant states that the need for some experimentation does not render the claimed invention unpatentable. A considerable amount of experimentation may be permissible if such experimentation is routinely practiced in the art. Applicant states that it has long been established that there is no statutory requirement for the disclosure of a specific example. In addition, Applicant asserts that as set forth by the Federal Circuit, the threshold of utility is not high, an invention is

useful under section 101 if it is capable of providing some identifiable benefit. Applicant cites case law.

Applicant's arguments have been fully considered but not deemed persuasive. Applicant cites in re Brana, however, it is unclear to the Examiner how this case is applicable to the argument at hand. The Patent and Trademark Office improperly rejected, for lack of utility, application claims for pharmaceutical compounds used in cancer treatments in humans. The full quote states, "usefulness in patent law, and in particular in the context of pharmaceutical inventions, necessarily includes the expectation of further research and development." "The stage at which an invention in this field becomes useful is well before it is ready to be administered to humans." This does not apply to the instant invention. In this case, the instant specification lists a number of disparate biological processes that Wnt-family proteins have been implicated in, such as blood cell formation, cancer, homeostasis, development, weight reduction, and inflammation. The specification fails to disclose any information regarding functional characteristics or mechanisms of action of WNT 14. There is no correlation to the predisposition of a specific disease or condition and WNT 14. The instant specification fails to disclose a direct correlation (working examples, animal models, etc.) between the use of the instant invention and treatment in subjects for a disease. The specification need not contain an example if the invention is otherwise disclosed in such manner that one skilled in the art will be able to practice it without an undue amount of experimentation. Lack of a working example, however is a factor to be considered, especially in a case involving an unpredictable and undeveloped art.

Furthermore, a considerable amount of time to make or use the invention based on the disclosure is permissible if it is merely routine or if the skilled artisan is give sufficient direction or guidance. However, the instant specification has failed to provide guidance as to how one of skill in the art could use the claimed invention in a way that constitutes a specific or substantial utility. The proposed uses of the claimed invention are simply starting points for further research and investigation into potential practical uses of the claimed polypeptide.

Applicant asserts that the requirements set forth in the Action for compliance with 35 USC 101 do not comply with the requirements suet forth by the Patent and Trademark Office itself for compliance with 35 USC 101. Applicant maintains that while they are aware of the new Utility Guidelines set forth by the USPTO, the current rules and regulations regarding the examination of patent applications is and always has been the patent laws as set forth in the 35 USC and the patent rules as set forth in 37 CFR, not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Applicant asserts that numerous patents have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines.

Applicant's arguments have been fully considered but not deemed persuasive. The current rejection is in compliance with the most currently published version of the Utility Guidelines, which require that all biological inventions must have credible, specific and substantial utility or a well established utility. Additionally, each Patent Application is examined on its own merits, what was allowable in one Patent has no bearing on this

Application. The scientific reasoning and evidence as a whole indicates that the rejection should be maintained.

Claim Rejections - 35 USC § 112, first paragraph

Claims 1-6 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at page 6 of the previous Office Action (20 February 2003, Paper No. 6).

Applicant maintains that as claims 1-4 have been shown to have a specific, substantial and credible utility, as detailed in section III above, the present rejection of claims 1-4 under 35 USC 112, first paragraph, cannot stand.

Applicant incorporates their response to the rejection under 35 USC 101 in response to the rejection under 35 USC 112, first paragraph. Applicants arguments have been fully considered but are not found persuasive for the reasons discussed above in the maintained rejection under 35 USC 101.

Conclusion

No claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Elizabeth C. Kemmerer

RMD
July 23, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER